

**AMENDMENTS TO THE SPECIFICATION:**

*Please replace the paragraph at page 12, lines 18-19 with the following replacement paragraph:*

**Figure 1A:** Nucleic acid sequence (A, SEQ ID NO: 1) of BACE455, and

**Figure 1B:** Amino amino acid sequence (B, SEQ ID NO: 2) sequence of BACE455 and alignment of amino acid sequence with BACE501 (SEQ ID NO: 36).

*Please replace the paragraph at page 12, lines 22-28 with the following replacement paragraph:*

**Figure 2 :** BACE455 (A, C) and BACE501 (B, D) immunolocalization. Immunolocalization on NIH 3T3 cells transfected with a construct expressing BACE455 or BACE501. A, B-Intracellular staining of BACE isoforms (BACE455, Fig. 2A; BACE501, Fig. 2B) on Triton X100- permeabilized cells using polyclonal anti-hBACE (481-501) (C-ter intracellular epitope). C,D-Extracellular staining of BACE isoforms (BACE455, Fig. 2C; BACE501, Fig. 2D) on non-permeabilized cells using polyclonal anti-hBACE (46-65) (N-ter extracellular epitope). Photomicrograph showing that BACE455 presents similar intracellular localization than BACE501, is efficiently exported to the cellular membrane where it displays comparable extracellular membranous immunoreactivity to BACE501.

*Please replace the paragraph at page 26, lines 12-24 with the following replacement paragraph:*

In addition to cleaving APP-based substrates, recombinant human BACE also cleaves a substrate with the sequence LVNM/AEGD (SEQ ID NO: 35) (Lin et al. Proc Natl Acad Sci U S A. 97(4):1456-1460 (2000)), a sequence which is the in vivo processing site sequence of human presenilins. Presenilin 1 and presenilin 2 are unstable proteins which are processed and subsequently stabilized by an unknown protease (Capell et al., J. Biol. Chem. 273, 3205 (1998); Thinakaran et al., Neurobiol. Dis. 4, 438 (1998)). It is known that presenilins control the formation of A- $\beta$  peptide by cleavage of APP at the gamma-secretase site, but also the activity of BACE. Presenilins therefore enhance the progression of Alzheimer's disease. Thus, the processing of presenilins by BACE would enhance the production of A- $\beta$  peptide and therefore, further stimulate the progress of Alzheimer's disease. Therefore, a BACE inhibitor would decrease the likelihood of developing or slow the progression of Alzheimer's disease by inhibiting APP cleavage at the beta-secretase site and/(or) by preventing the processing of presenilins, thus indirectly inhibiting APP cleavage at the gamma-secretase site.